

## **Remarks/Arguments**

### Amendments to the Claims

Support for the amended claim language of claim 1 and new claims 17-21 is found on page 8, lines 16-20, Examples 3 and 4 and Figures 3, 4, 5, 6 and 8.

Support for new claims 15 and 16 is found on page 14, lines 17-22.

Applicant submits that no new matter is presented with these amendments.

### Sequence Compliance

A sequence listing complying with the requirements of 37 C.F.R. §§ 1.821(a)(1) and (a)(2) and a copy of the Notice to Comply are attached.

### Information Disclosure Statement

Applicant attests that the references referred to in the information disclosure statement filed on May 20, 2004 were previously submitted to the United States PTO in a supplemental disclosure statement filed February 10, 2003. A copy of this filing was re-sent to the PTO via fax on September 27, 2004. Thus, Applicant submits that it has complied with the requirements of 37 C.F.R. §1.98. **Applicant requests that the Examiner initial and return to us a copy of the PTO form 1449 submitted February 10, 2003 and resent September 27, 2004.**

### Rejections under 35 U.S.C. §102

Claims 1, 2, 4, 5, 11, 12 and 14 are rejected as being anticipated under 35 U.S.C. §102 by Harney (U.S. Pat. No. 6,495,318). This rejection is rendered moot in light of current amendments to claims. Specifically, Harney discloses a method of assembling a nucleic acid

multicomponent construct from component nucleic acid molecules, and is replete with the teaching that each of component nucleic acid molecules comprises a functional genetic unit or portion of a genetic unit. See, for example Column 7, lines 18-22 (“The nucleic acid sequences contained within each nucleic acid component provide the requisite information for *a specific biological function or functions* or for a specific utility deemed essential by the user”), Column 12, lines 40-42 (“According to the method [of this invention], the vector is assembled from nucleic acid components providing *a single functionality or multiple functionalities* as appropriate”), and Column 25, lines 16-18 (“Each nucleic acid component involved in the assembly of a vector construct is intended to encode *a specific biological functionality or multiple functionalities*”) (emphasis added). Harney does not teach a method of preparing a vector by providing at least two collections of vector fragments, wherein each vector fragment in each of the collections contains a portion of a vector element which cannot alone provide a function, but which function is reconstituted when a vector fragment from each collection is ligated together, as currently recited in claim 1. Since Harney does not disclose each and every element of the claims as currently amended, the currently pending claims cannot be anticipated by the teachings of Harney.

Applicant respectfully requests that the Examiner withdraw this rejection.

### Rejections under 35 U.S.C. §103

Claims 1-5 and 11-14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Harney (U.S. Pat. No. 6,495,318) in view of Jarrell (US Pat. No. 5,498,531) or Jarrell (US Pat. No. 5,780,272). This rejection is rendered moot in light of current amendments to claims.

Harney teaches method of assembling a nucleic acid multicomponent construct from component nucleic acid molecules by annealing double stranded nucleic acid molecules that contain complementary 5' or 3' terminal sequences. Although Harney discloses that some of the component nucleic acid molecules may contain exon and intron sequences, he fails to teach a method of assembling nucleic acid multicomponent constructs that takes advantage of the ability of intron elements to splice. Instead, he teaches that double stranded nucleic acid molecules containing exon and intron sequences and that have terminal 5' or 3' overhangs may be admixed, producing a new double stranded construct (column 18, lines 4-28). This new construct is then cloned into an expression vector (column 18, lines 29-30). Upon transcription, the cloned intron sequences mediate intramolecular splicing to generate an RNA molecule that lacks the excised intron (column 18, lines 37-39). Thus, the splicing event taught by Harney takes place after the component nucleic acid molecules have been joined and occurs within a single transcript produced by the resulting joined molecule.

In contrast, Jarrell teaches a method of linking nucleic acids containing intron sequences that are able to direct site-specific trans-splicing between two discontinuous nucleic acids. In the method taught by Jarrell, discontinuous single-stranded RNA molecules that contain flanking intron sequences capable of directing trans-splicing are incubated together. The flanking intron sequences then direct trans-splicing of the two discontinuous molecules. As a result, the two discontinuous molecules are joined together into a single continuous molecule that lacks the excised flanking intron sequences.

Despite the Examiner's assertion that it would have been obvious to combine the teachings of Jarrell to the method of Harney in order to efficiently manipulate nucleic acids by cleavage and ligation, there is no suggestion or motivation in the prior art or elsewhere to combine the two methods. Instead, it is only Applicant's disclosure that teaches that the trans-

splicing of two discontinuous nucleic acid molecules as taught by Jarrell can be applied to the method of preparing a vector by providing at least two collections of vector fragments, wherein each vector fragment in each of the collections contains a portion of a vector element which cannot alone provide a function, but which function is reconstituted when a vector fragment from each collection is ligated together, as currently recited in claim 1. It is well settled that a suggestion or motivation to combine is required in order to levy an obviousness rejection under 35 U.S.C. §103. See In re Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999) (“Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references”).

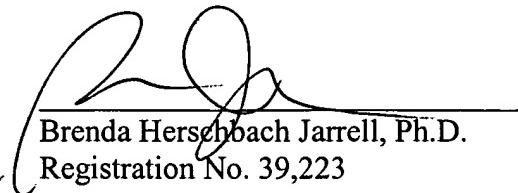
Furthermore, even if the teachings of Harney and Jarrell were combined, such a combination would not result in the method recited in the pending claims. The present claims recite a method of preparing a vector by providing at least two collections of vector fragments, wherein each vector fragment in each of the collections contains a portion of a vector element which cannot alone provide a function, but which function is reconstituted when a vector fragment from each collection is ligated together. Neither Harney nor Jarrell, alone or in combination, teach or suggest each and every element of this method and thus cannot render the currently pending claims obvious.

Applicant respectfully requests that the Examiner withdraw this rejection.

In light of these Remarks and Amendments, Applicant respectfully submits that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

Applicant believes that no fees are associated with this response. However, please charge any applicable fees, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully Submitted,



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